

WHAT IS CLAIMED IS:

1. An isolated and purified nucleic acid molecule that encodes a mammalian histamine H₄ receptor protein, said nucleic acid molecule comprising a member

5 selected from a group consisting of:

(a) a nucleic acid molecule encoding a protein having at least 70% identity to a polypeptide comprising amino acids 1 to 390 of SEQ ID NO:2;

(b) a nucleic acid molecule which is complementary to the polynucleotide of (a);

10 (c) a nucleic acid molecule comprising at least 15 sequential bases of the polynucleotide of (a) or (b);

(d) a nucleic acid molecule that hybridizes under stringent conditions to the polynucleotide molecule of (a);

15 (e) a nucleic acid molecule encoding a protein having at least 70% identity to a polypeptide comprising amino acids 1 to 391 of SEQ ID NO:8;

(f) a nucleic acid molecule which is complementary to the polynucleotide of (e);

(g) a nucleic acid molecule comprising at least 15 sequential bases of the polynucleotide of (f) or (e);

20 (h) a nucleic acid molecule that hybridizes under stringent conditions to the polynucleotide molecule of (e);

(i) a nucleic acid molecule encoding a protein having at least a 70% identity to a polypeptide comprising amino acids 1 to 391 of SEQ ID NO:9;

(j) a nucleic acid molecule which is complementary to the polynucleotide of

(i);

5 (k) a nucleic acid molecule comprising at least 15 sequential bases of the polynucleotide of (i) or (j);

(l) a nucleic acid molecule that hybridizes under stringent conditions to the polynucleotide molecule of (i);

10 (m) a nucleic acid molecule encoding a protein having at least a 70% identity to a polypeptide comprising amino acids 1 to 389 of SEQ ID NO:10;

(n) a nucleic acid molecule which is complementary to the polynucleotide of (m);

15 (o) a nucleic acid molecule comprising at least 15 sequential bases of the polynucleotide of (m) or (n); and

(p) a nucleic acid molecule that hybridizes under stringent conditions to the polynucleotide molecule of (m).

2. The nucleic acid molecule of claim 1 wherein the polynucleotide is RNA.

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3. The nucleic acid molecule of claim 1 wherein the polynucleotide is DNA.

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4. The isolated and purified nucleic acid molecule of claim 1, having a nucleotide sequence selected from a group consisting of: (SEQ.ID.NO.:1), (SEQ.ID.NO.:5), (SEQ.ID.NO.:6), and (SEQ.ID.NO.:7).

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5. The isolated and purified nucleic acid molecule of claim 1, wherein said nucleic acid molecule is genomic DNA.

6. An expression vector for expression of a mammalian histamine H4 receptor protein in a recombinant host, wherein said vector contains a nucleic acid sequence encoding a mammalian histamine H4 receptor protein.

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7. The expression vector of claim 6, wherein the expression vector contains a nucleic acid molecule encoding a mammalian histamine H4 receptor protein having a nucleotide sequence selected from a group consisting of: (SEQ.ID.NO.:1), (SEQ.ID.NO.:5), (SEQ.ID.NO.:6), or (SEQ.ID.NO.:7).

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8. The expression vector of claim 6, wherein the expression vector contains genomic DNA encoding a mammalian histamine H4 receptor protein.

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9. A recombinant host cell containing a recombinantly cloned nucleic acid molecule encoding a mammalian histamine H4 receptor protein.

10. The recombinant host cell of claim 9, wherein said nucleic acid molecule
5 has a nucleotide sequence selected from a group consisting of: (SEQ.ID.NO.:1);
(SEQ.ID.NO.:5), (SEQ.ID.NO.:6), and (SEQ.ID.NO.:7).

11. The recombinant host cell of claim 9, wherein said cloned nucleic acid molecule is genomic DNA.

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12. A protein in substantially pure form that functions as mammalian histamine H4 receptor protein.

13. The protein according to claim 12, having an amino acid sequence
15 selected from a group consisting of: (SEQ.ID.NO.:2), (SEQ.ID.NO.:8),
(SEQ.ID.NO.:9), and (SEQ.ID.NO.:10).

14. A monospecific antibody immunologically reactive with a mammalian histamine H4 receptor protein.

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15. The antibody of Claim 14, wherein the antibody blocks activity of the mammalian histamine H4 receptor protein.

16. A process for expression of mammalian histamine H4 receptor protein in a recombinant host cell, comprising:

- (a) transferring the expression vector of Claim 6 into suitable host cells; and
- (b) culturing the host cells of step (a) under conditions which allow expression of the mammalian histamine H4 receptor protein from the expression vector.

17. A method of identifying compounds that modulate mammalian histamine H4 receptor protein activity, comprising:

- (a) combining a putative modulator of mammalian histamine H4 receptor protein activity with mammalian histamine H4 receptor protein; and
- (b) measuring an effect of the modulator on the protein.

18. The method of claim 17, wherein the effect measured in step (b) is competition between the modulator of step (a) with a known ligand of the histamine H4 receptor for binding to the receptor.

19. The method of claim 17, wherein the effect measured in step (b) is modulation of a histamine H4 receptor intracellular second messenger.

20. The method of claim 19, wherein the intracellular second messenger is selected from a group consisting of cAMP, calcium, and a reporter gene product.

5 21. A compound identified using the method of Claim 17, wherein said compound is a modulator of a mammalian histamine H4 receptor.

22. A compound identified using the method of Claim 17, wherein said compound is an agonist, antagonist, or inverse agonist of a mammalian histamine H4 receptor.

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23. A compound identified using the method of Claim 17, wherein said compound modulates the expression of the mammalian histamine H4 receptor protein.

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24. A pharmaceutical composition comprising a compound active in the method of Claim 17 and a pharmaceutically acceptable carrier.

25. A method of treating a patient in need of such treatment for a condition that is mediated by a histamine H4 receptor comprising administration of a pharmaceutical composition of claim 24.

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